Bentley Patent Estate

TRANSDERMAL AND TRANS-MEMBRANE DELIVERY PATENTS.

- US Patent # 5,023,252, June 11, 1991 - Transdermal and Trans-Membrane Delivery of Drugs (Hsieh Patent). 11 other international patents obtained: Belgium, Canada, Denmark, France, Germany, Great Britain, Italy, Japan, Korea, Luxembourg and Switzerland.
- PCT/US03/12235 filed April 21, 2003 (priority date April 19, 2002) - Transdermal Delivery of Testosterone in Hypogonadal Men. PCT application and selected other countries filed; national filings in process.

ANTIFUNGAL NAIL LACQUER PATENTS

- US Patent 6,495,124, December 17, 2002 (Acquired from Macrochem in July 2003).
- PCT/US01/05302, WO 01/60325 A1, published August 23, 2001 - Lacquer administration of pharmaceutical products utilizing enhancer permeation. PCT application and selected other countries filed; national filings in process.

MUCOSAL DELIVERY PATENTS

- application being drafted by patent counsel for PCT submission.

HYDROGEL PATENTS

- US Patent # 4,983,393, January 8, 1991 - Intra vaginal device and methods for sustained release.
- US Patent # 5,069,906, December 3, 1991 - Intra-vaginal device.

PARACETAMOL PATENTS

- PCT # 200002653, filed March 11, 2000. New dispersible and soluble galenic formulation of paracetamol, process for its preparation and applications. National applications filed in European Patent Office, U.S., Japan and Poland.

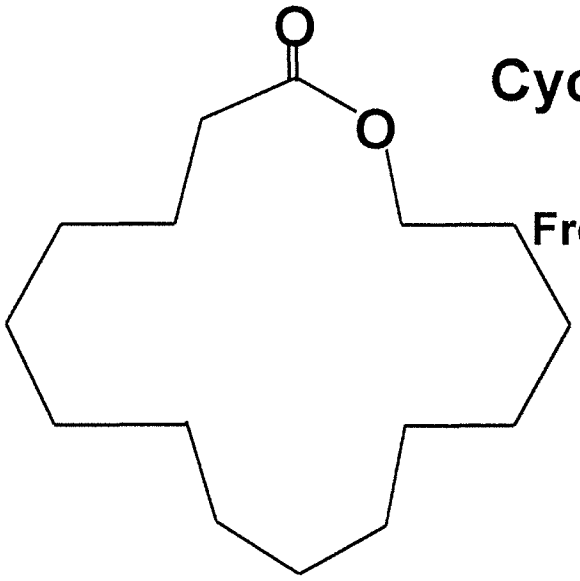
OMEPRAZOLE / LANSOPRAZOLE PATENTS

- Spain application filed April 29, 2003; to be filed with PCT – Improved process for manufacture of pellets of omeprazole, lansoprazole and other pharmaceutical products.

Bentley Topical Drug Delivery

CPE-215

Bentley Permeation Excipient



Cyclopentadecanolide (CPE-215)
Oil of Angelica Essence

From the root of Angelica archangelica

B631

CPE-215 – application examples

Compatible formats: gel, cream, ointment, patch, tablet, capsule, liquid, lacquer

- ⇨ Topical finger/toe nail penetration
- ⇨ Topical dermal – local effect
- ⇨ Topical dermal – systemic effect
- ⇨ Ophthalmic
- ⇨ Oral absorption enhancement
- ⇨ Nasal – systemic effect
- ⇨ Compatible with 'patch' constituents

B632

Advantages of CPE-215

- GRAS Excipient for food and cosmetic use
  - Approved by FDA as a Direct Food Additive (21 CFR 172.515)
  - Approved as a Fragrance
  - Approved as a Flavor Enhancer
- Excellent Transdermal Enhancement
  - Format Independent, i.e. effective in Patches, Gels, Ointments, Lotions, Creams
  - Compatible With Most Materials, Including Adhesives
- Non Irritating
- Stable excipient
- Available 99^{+}% under food & cosmetic GMP

B633

Topical Delivery with CPE-215
Clinical studies

Hormone Replacement: male hypogonadism

Testim® (Auxilium Pharma) – Plasma Testosterone

Table 1. Geometric mean (CV_b%) C_{max} and AUC_{0-24} for testosterone

	C_{max} (ng/dl)	AUC_{0-24} (ng*h/dl)
Testim™	480 (70.3)	5864.5 (77.9)
AndroGel®	368 (60.9)	4499.1 (77.9)

Biopharm. Drug Dispos. 24: 115–120 (2003)

"The ratio of the treatment comparison for both Cmax and AUC 0-24 was 1.30, indicating that [serum] values for Testim® were 30% greater than for AndroGel®. The 90% confidence interval for Cmax ratio was (1.10, 1.55), and for AUC 0-24 it was (1.08, 1.57). Since neither of these confidence intervals was wholly contained within the bioequivalence limits of 0.80 to 1.25, Testim® and AndroGel® are not bioequivalent." Copyright # 2003 John Wiley & Sons, Ltd. Biopharm. Drug Dispos. 24: 115–120 (2003)

Testim® (Auxilium Pharma) - Plasma DHT

Table 2. Median (range) C_{max} and AUC_{0-24} for dihydrotestosterone[a]

	C_{max} (pg/ml)	AUC_{0-24} (pg·h/ml)
Testim™	321 (23–964)	4891.0 (257.5–15259.1)
AndroGel®	313 (16–1038)	4091.7 (225.0–16044.5)

[a] Excluding one patient for AUC_{0-24} because there was insufficient sample volume for analysis in Period 2.

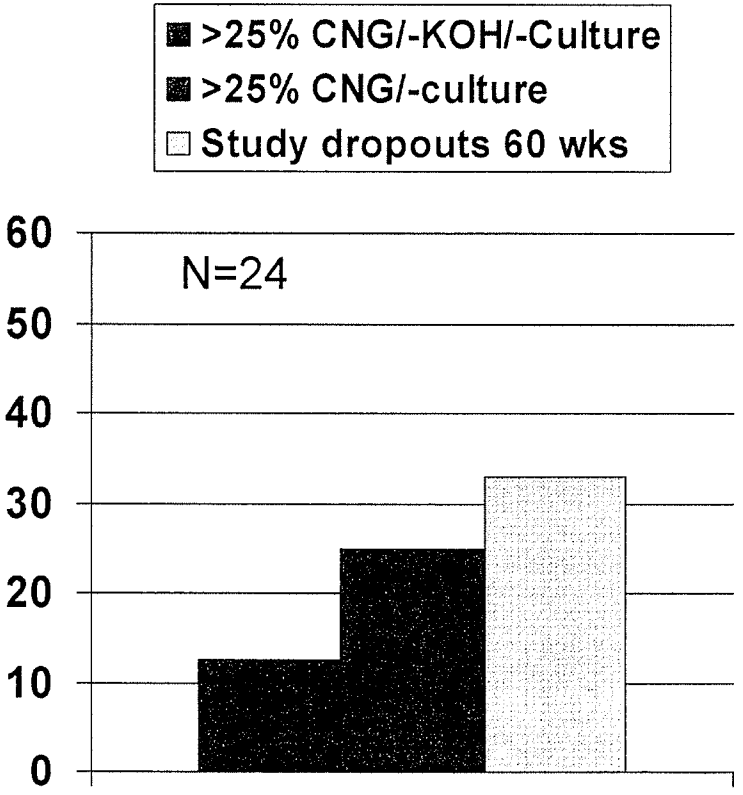
"For both Cmax and AUC 0-24, median values for Testim® were greater than for AndroGel® (seeTable 2). For Cmax, the estimated treatment ratio was 1.19, indicating that values for Testim® were greater than for AndroGel®. Similarly for AUC 0-24, the estimated treatment ratio was 1.11. The 90% confidence interval for Cmax ratio was (0.91, 1.36), and (0.95, 1.32) for AUC0-24. As neither of these confidence intervals was wholly contained within the bioequivalence limits of 0.80 to 1.25, Testim® and AndroGel® are not bioequivalent."

Nail fungal infection: Onychomycosis

Bentley Pharmaceuticals, Inc.

Toenail Onychomycosis

4% Clotrimazole with 15% CPE



48 weeks treatment with 12 weeks follow-up

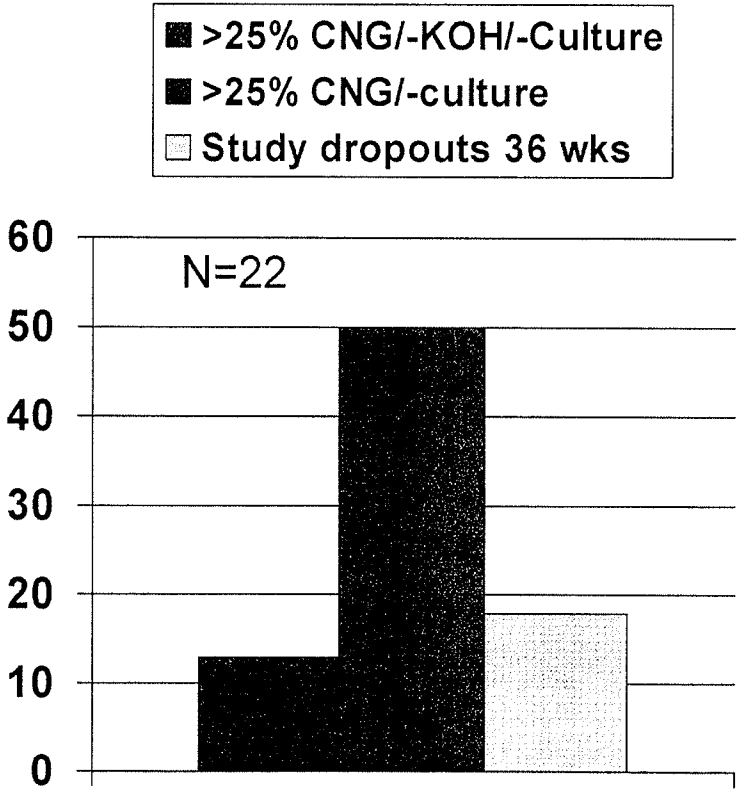
Patients with:

- 25-100% Clear Nail Growth & (-)KOH & (-) Culture at 60 weeks = 12.5% (3/24)
- 25-150% Clear Nail Growth & (-)Culture at 60 weeks = 25% (6/24)

Noncompleters/Drop outs in study by 60 weeks = 33% (8/24)

Fingernail Onychomycosis

4% Clotrimazole with 15% CPE



24 weeks treatment with 12 weeks follow-up

Patients with:

- 25-350% Clear Nail Growth & (-)KOH & (-)Culture at 36 weeks = 13% (3/22)
- 20-400% Clear Nail Growth & (-)Culture at 36 weeks = 50% (11/22)

Noncompleters/Drop outs in study by 36 weeks = 18% (4/22)

Diabetes: Intranasal Insulin

Nasal Insulin

- Pig data
- Human clinical – insert slide(s)
  - Phase I Efficacy & Safety

CPE-215 topical products pipeline

	Preclinical	Ph I	Ph II	Ph III	Mkt
Onychomycosis	Terbinafine lacquer		Clotrimazole lacquer		
Diabetes		Nasal Insulin			
Hormonal steroids	Estradiol gel Androgenic gel*				Testim® gel*
Severe pain	Nasal narcotic*				
Ophthalmic	Indomethacin Timolol				
Antiinflammatory	Diclofenac gel				
Antifungal	Itraconazole gel Ketoconazole gel				

* In partnership with Auxilium Pharmaceuticals Inc.

Bentley Pharmaceuticals, Inc.

Bentley Generics and Improved Generics

Bentley Improved products

Soluble Acetaminophen

By Laboratorios BELMAC, S.A.
Wholly owned subsidiary of Bentley Pharmaceuticals, Inc.

Bentley Pharmaceuticals, Inc.

Soluble Acetaminophen

OBJECTIVE:

To develop a new manufacturing process:

- High dissolution rate
- High absorption rate
- Good taste
- Low cost

Pharmaceutical Formats

- Sachets
- Fast Dissolve Swallow Tablets

Overall Pharmacokinetic parameters of 5 formulations studied: No Differences

A = 2 x 500-mg paracetamol tablets (Laboratorios Belmac S.A)
B = 1 x 1000-mg paracetamol powder sachets (Laboratorios Belmac, S.A.)
C = 2 x 500-mg paracetamol film-coated tablets (Panadol® ,SmithKline Beecham)
D = 2 x 500-mg paracetamol tablets (Tylenol®, McNeil)
E = 1 x 1000-mg effervescent paracetamol tablets (Efferalgan®, UPSA).

Parameter	Formulation				
	A	B	C	D	E
$AUC_{0-\infty}$ ($\mu_{g.h/ml}$)	55.4 (10.3) [18.6%]	52.6 (12.5) [23.8%]	54.8 (14.4) [26.4%]	56.3 (14.9) [26.5%]	53.4 (11.7) [21.9%]
$AUC_{0\text{-}tlast}$ (μg.h/ml)	53.3 (10.5) [27.6%]	50.8 (12.4) [24.4%]	52.7 (14.5) [27.6%]	53.9 (15.0) [27.8%]	51.8 (11.9) [22.9%]
C_{max} (μg/ml)	20.55 (6.90) [33.6%]	20.24 (6.22) [30.8%]	17.98 (6.21) [34.5%]	19.41 (7.60) [39.2%]	20.73 (5.76) [27.8%]
$t_{1/2}$ (h)*	2.81 (2.41) [65.5%]	2.81 (1.05) [33.9%]	2.65 (0.73) [25.2%]	2.68 (1.58) [47.4%]	2.71 (0.72) [24.9%]

Data shown are mean (standard deviation) [coefficient of variation]. *, median values.
$AUC_{0-\infty}$, area under the plasma concentration time curve extrapolated to infinity;
$AUC_{0\text{-}tlast}$, area under the plasma concentration time curve from 0-t hours after drug administration
C_{max}, maximum plasma concentration
$t_{1/2}$, terminal elimination half-life.
N = 12.

Temporal pharmacokinetic parameters of 5 formulations studied.

Parameter	Formulation				
	A	B	C	D	E
$AUC_{0\text{-}0.25h}$ (µg.h/ml)	**2.16** (1.26) [58.5%]	**2.36** (1.01) [42.83%]	0.55 (0.71) [129.92%]	1.07 (1.35) [125.73%]	**2.31** (0.90) [38.88%]
$AUC_{0\text{-}0.50h}$ (µg.h/ml)	**6.16** (2.89) [46.99%]	**6.73** (2.46) [36.61%]	2.78 (2.25) [80.75%]	4.02 (2.93) [72.88%]	**6.48** (1.69) [26.06%]
$AUC_{0\text{-}0.75h}$ (µg.h/ml)	9.45 (3.70) [39.09%]	10.32 (3.08) [29.84%]	6.04 (3.95) [65.51%]	7.48 (3.82) [51.10%]	9.72 (2.15) [22.11%]
$AUC_{0\text{-}1.0h}$ (µg.h/ml)	13.14 (3.70) [28.15%]	13.33 (3.41) [25.58%]	9.01 (5.12) [56.88%]	10.61 (4.45) [41.91%]	13.21 (2.40) [18.17%]
$C_{0.25h}$ (µg/ml)	**17.02** (10.11) [59.40%]	**18.63** (8.09) [43.40%]	4.14 (5.71) [137.76%]	8.60 (10.55) [122.69%]	**18.25** (7.19) [39.41%]

A = 2 x 500-mg paracetamol tablets (Laboratorios Belmac S.A)
B = 1 x 1000-mg paracetamol powder sachets (Laboratorios Belmac, S.A.)
C = 2 x 500-mg paracetamol film-coated tablets (Panadol® ,SmithKline Beecham)
D = 2 x 500-mg paracetamol tablets (Tylenol®, McNeil)
E = 1 x 1000-mg effervescent paracetamol tablets (Efferalgan®, UPSA).

Data shown are mean (standard deviation) [coefficient of variation].

$AUC_{0\text{-}0.25h}$, area under the plasma concentration time curve 15 minutes after dosing;
$AUC_{0\text{-}0.5h}$, area under the plasma concentration time curve 30 minutes after dosing;
$AUC_{0\text{-}0.75h}$, area under the plasma concentration time curve 45 minutes after dosing;
$AUC_{0\text{-}1.0h}$, area under the plasma concentration time curve one hour after dosing;
$C_{0.25h}$, plasma concentration at 15 minutes after dosing. For all results, n = 12.

Bentley Pharmaceuticals, Inc.

Summary t_{max} data (hours) for 5 formulations studied

Formulation	Mean	Min - Max	Median
A (2 x 500-mg paracetamol tablets; Laboratorios Belmac S.A)	**0.44** (0.19) [43.1%]	0.25 – 0.75	0.50
B (1 x 1000-mg paracetamol powder sachets; Laboratorios Belmac, S.A.)	**0.44** (0.28) [65.0%]	0.25 – 1.00	0.25
C (2 x 500-mg paracetamol film-coated tablets; Panadol®, SmithKline Beecham)	0.88 (0.55) [62.1%]	0.50 – 2.00	0.50
D (2 x 500-mg paracetamol tablets; Tylenol®, McNeil)	0.80 (0.76) [95.8%]	0.25 – 3.00	0.50
E (1 x 1000-mg effervescent paracetamol tablets; Efferalgan®, UPSA)	**0.40** (0.17) [42.2%]	0.25 – 0.75	0.38

Mean data are shown as arithmetic means with (standard deviation) and [coefficient of variation], N = 12.

Bentley Generics

B650

Bentley Generics

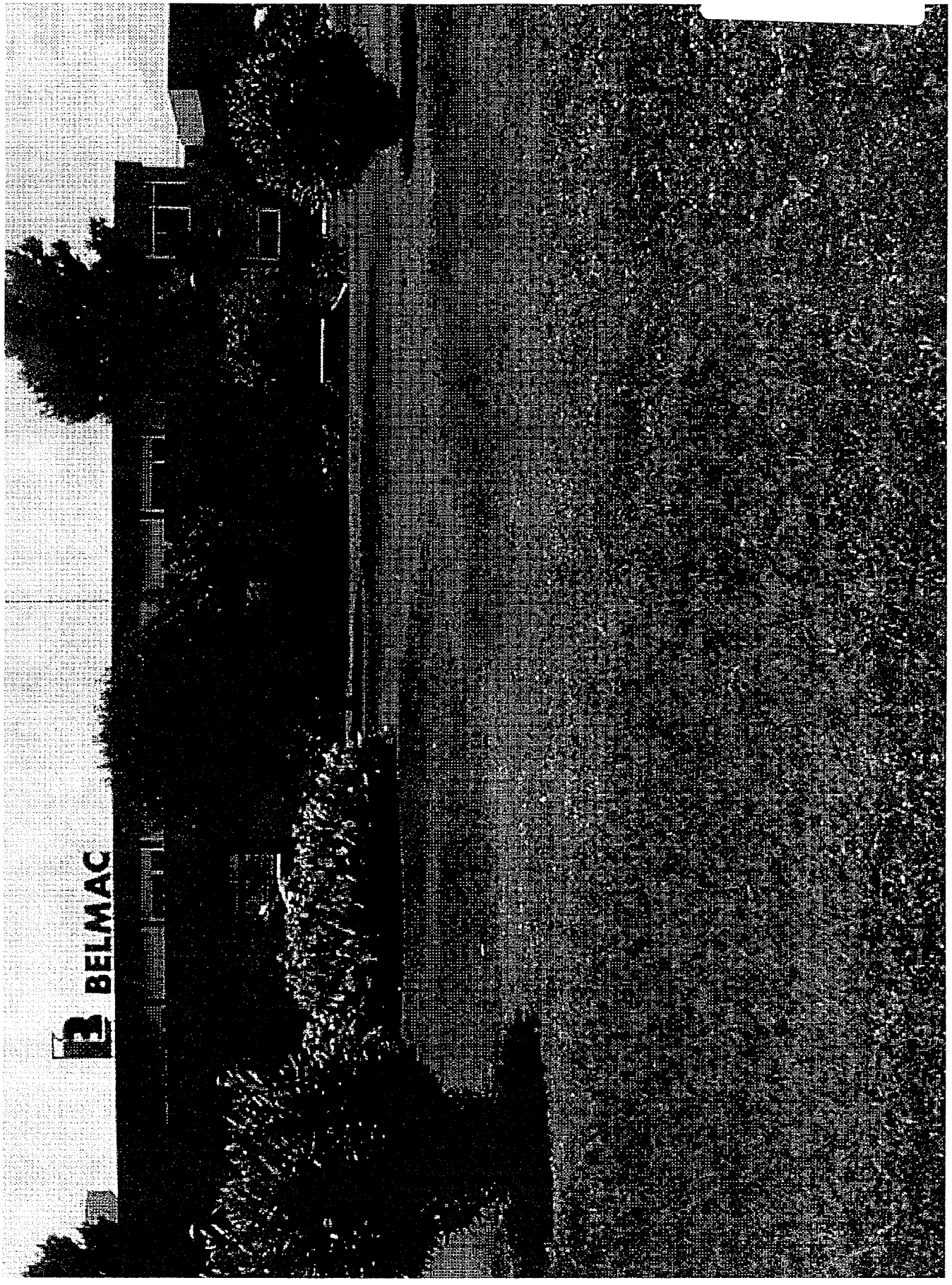
- Add slides
- Business in Spain
  - ⇨ GMP Facility
  - ⇨ Hi Capacity – Low Costs
- Partnership with Teva for Spain
- Business Outside Spain
- Registrations Owned by Bentley
- US Plans

Facilities in Zaragosa Spain

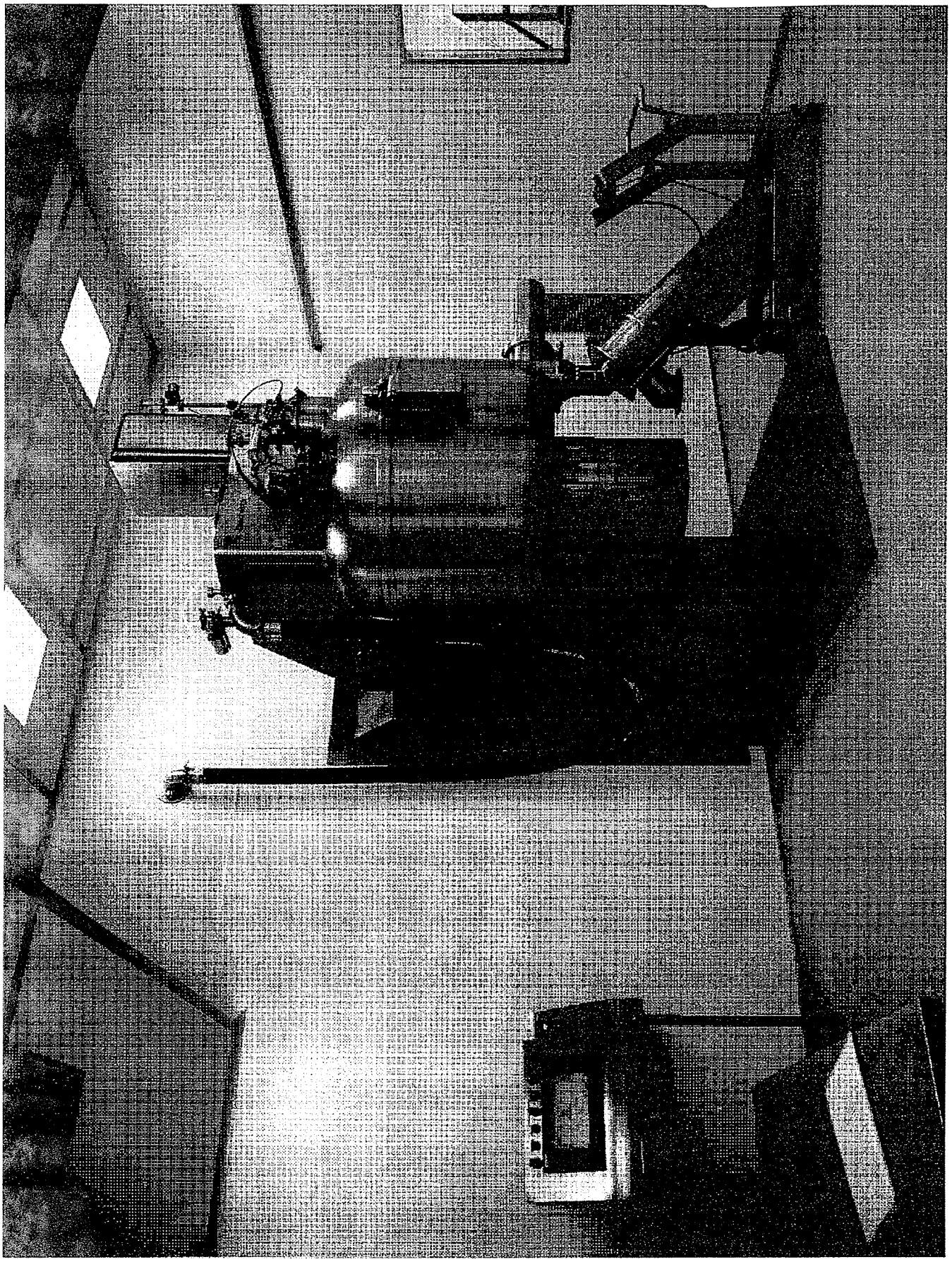
Bentley Pharmaceuticals, Inc.

B652

B653



B654



B655

Bentley
Pharmaceuticals, Inc.

SIDE LETTER

TO THE AGREEMENT

BETWEEN LECIVA A.S. AND UQUIFA S.A.

TO BE CONCLUDED IN JANUARY, 2003

OMEPRAZOLE PELLETS

Whereas Leciva a.s., U Kabelovny 130, 102 37 Prague, Czech Republic, concluding the above mentioned Agreement wish to specify more thoroughly several clauses and to specify their relation to Laboratorios Belmac S.A., C Teide 4, Planta Baja, Polígono Empresarial La Marina, 28700 Madrid, Spain, the producer of Omeprazole Pellets, Belmac and Leciva agreed to sign this Side Letter.

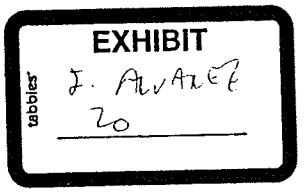
1. Belmac declares that it produces Omeprazole Pellets according to its own technology and documentation which does not breach any third parties rights, namely that of Ethypharm.

2. Belmac declares that Omeprazole Pellets are produced by its own equipment and/or third parties equipment used under consent of the said third party.

3. Belmac shall indemnify and hold Leciva harmless and its employees and agents from any and all liabilities, claims, demands, actions, suits, losses, damages, costs and expenses (including reasonable attorney's fees) resulting from any third parties claims in respect of clauses 1 and 2 mentioned hereinabove which may be made or brought against Leciva.

4. Belmac declares that the composition of Omeprazole Pellets is the same as that delivered to Leciva in the past and that it is in accordance with a Declaration issued on 5/6/2000 attached to this Side Letter. In the event that Leciva needs an official declaration for the health governmental regulatory authorities that Belmac is manufacturing the goods with unchanged composition; Belmac shall without any delay issue such a declaration and forward it to Leciva.

5. Belmac commits itself to deliver free of charge and not later than by the end of April 2003 an English version of an EU dossier on aqueous formulation in CTD format complying with current EU guidelines. 18 months stability data shall be delivered not later than by 30th November 2003.



SIGNED by:

Laboratorios Belmac S.A.

Madrid, _____, 2002

Adolfo Herrera Málaga

General Manager

SIGNED by:

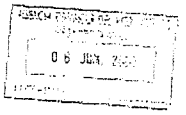
LECIVA a.s.

Praha, _____, 2002

Jan Sotola

Director Strategic Sourcing

Laboratorios Belmac, S.A.



AGENCIA ESPAÑOLA DEL MEDICAMENTO
SUBDIRECCION GENERAL DE SEGURIDAD DEL MEDICAMENTO
C/ Huertas 75
28014 MADRID

D. Juan Carlos Avenso Asensio, como Director Tecnico Farmaceutico de Laboratorios Belmac, S.A., inscrito en la Dirección General de Farmacia y Productos Sanitarios con el nº 2150, con domicilio en C/ Monenegros,9, 1º., 28037 MADRID y fábrica en Polígono de Malpica C/ C nº4, 50016 ZARAGOZA, por la presente,

MANIFIESTA:

1.- Que Laboratorios Belmac, S.A. tiene autorizado por la Agencia Española del Medicamento con fecha 12 de Abril de 2000, la fabricación de cápsulas de microgránulos de Omeprazol, a granel, y su exportación a Laboratorios LECIVA, con domicilio en Dalmi Mechelupy 150, 40247 PRAHA 10, REPÚBLICA CHECA.

2.- Que el llenado y cerrado de las cápsulas se realiza de acuerdo con las normas oficiales de buena manufactura (G.M.P.).

3.- Que deseamos exportar 500.000 cápsulas del lote P11LE y conforme a Decreto de 23 de Diciembre de 1983, le comunicamos

Para que conste, firmo la presente en Madrid a 2 de Junio de 2000

Fdo.: Juan Carlos Asensio Asensio
Director Técnico Farmacéutico

BELMAC

Barrier Therapeutics

2 Oct 2003

Bentley Pharmaceuticals, Inc.

Bentley operations

Bentley HQ – Exeter NH, USA

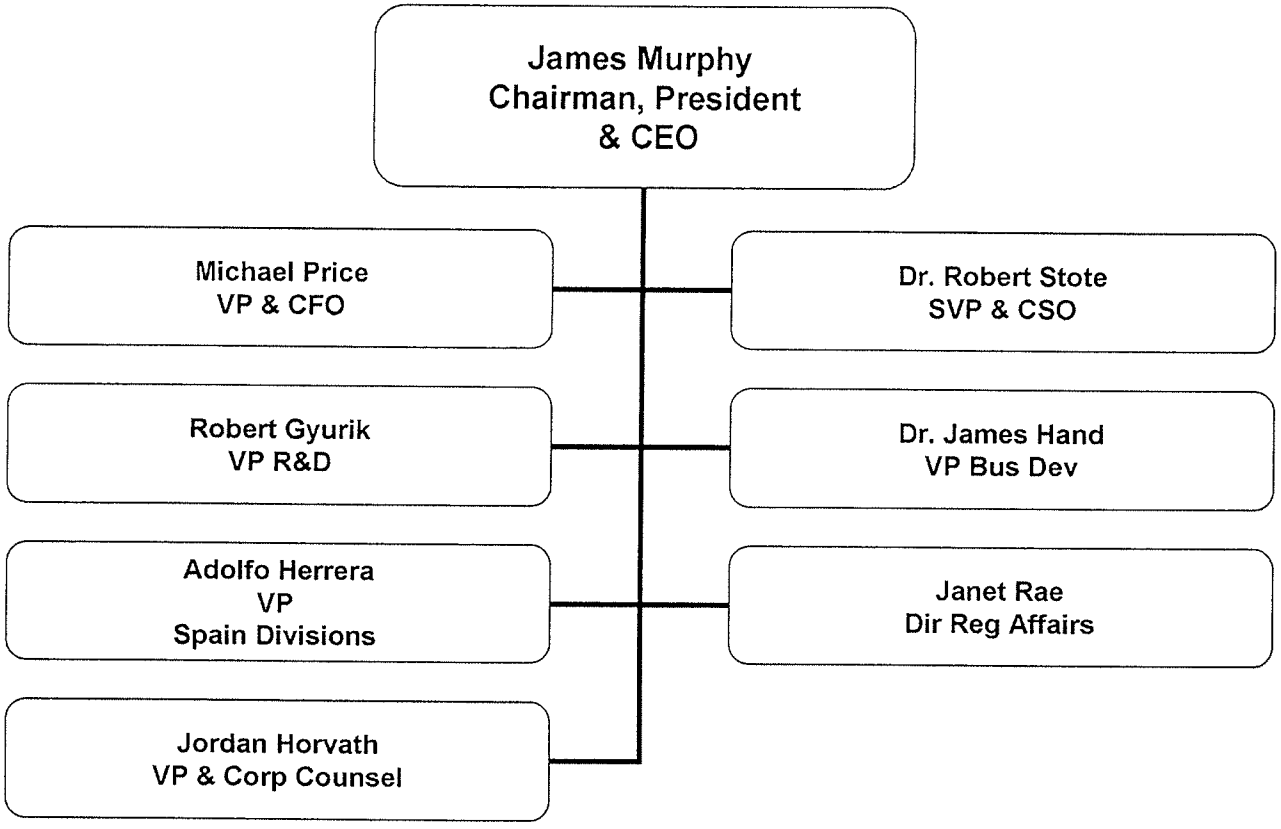
Bentley Divisions

- Belmac – Zaragosa & Madrid, Spain - Branded
- Rimafar – Madrid, Spain - OTC's
- Davur – Madrid, Spain - Generics

www.bentleypharm.com

B660

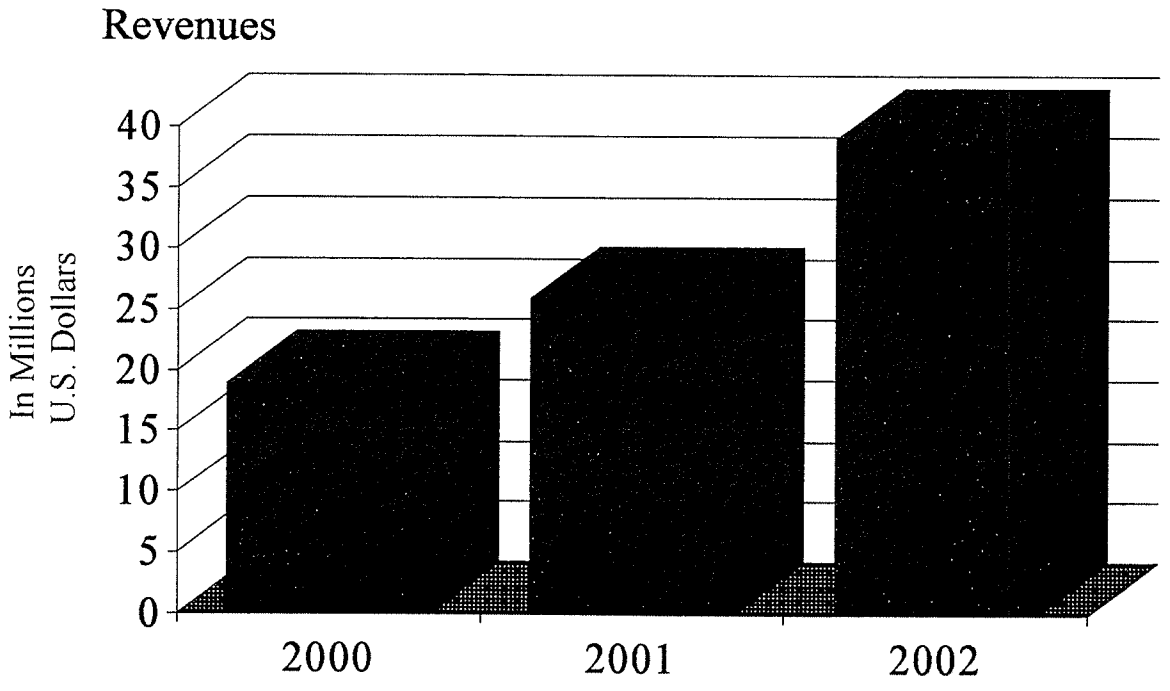
Bentley management



Financial Highlights

Consistent Revenue Growth

Historical Performance



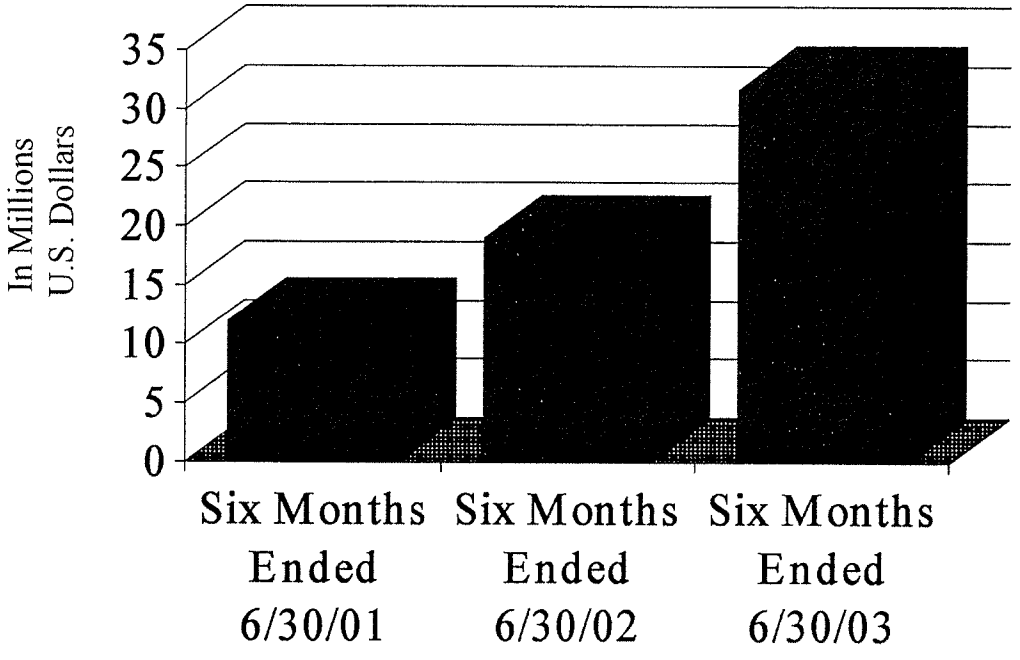
Bentley Pharmaceuticals, Inc.

Financial Highlights

Consistent Revenue Growth

Current Period Performance

Revenues



Bentley Pharmaceuticals, Inc.

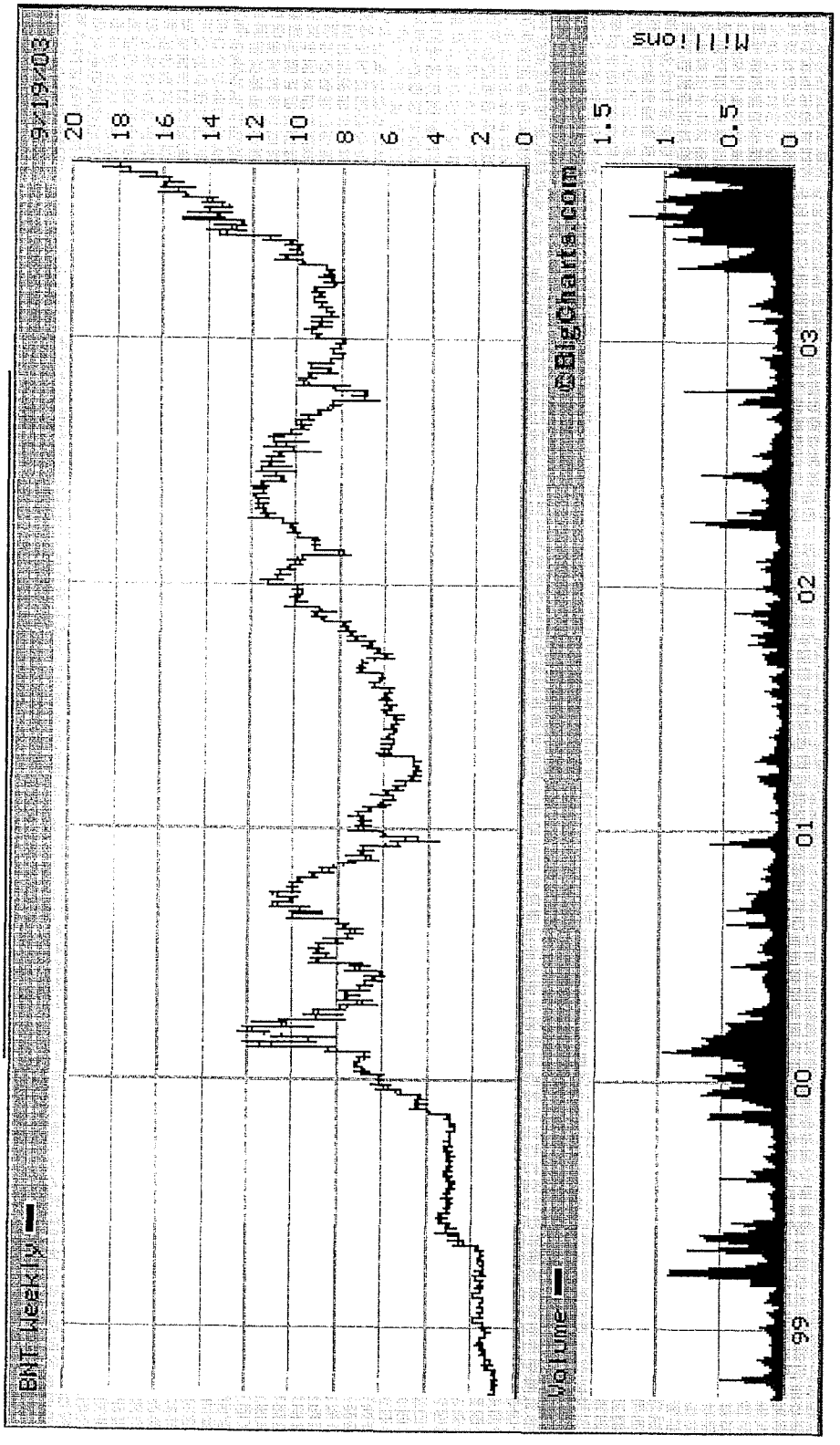
Financial Highlights

Strong Balance Sheet

Selected Balance Sheet Data

	December 31,		
	2002	2001	2000
Working capital	$30,703	$6,276	$3,742
Non-current assets	20,720	16,280	15,773
Total assets	64,692	32,119	28,877
Non-current liabilities	2,672	2,132	1,699
Stockholder's equity	48,751	20,424	17,816

Stock performance



Bentley Pharmaceuticals, Inc.

Bentley Patents Estate

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- US Patent # 5,025,252 , June 11, 1991 - Transdermal and Trans-Membrane Delivery of Drugs (Hsieh Patent). 11 other international patents obtained: Belgium, Canada, Denmark, France, Germany, Great Britain, Italy, Japan, Korea, Luxembourg, and Switzerland.
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ANTIFUNGAL NAIL LACQUER PATENTS

- PCT/US01/05302, WO 01/60325 A1, published 23 August 2001 - Lacquer administration of pharmaceutical products utilizing enhancer permeation. Also filed world-wide through PCT application.
- US Patent 6,495,124, December 17, 2002 (Acquired from Macrochem in July 2003).

MUCOSAL DELIVERY PATENTS

- PCT/US02/19849, filed June 24, 2002 - Intranasal/Mucosal Delivery. Filed world-wide through PCT application.

HYDROGEL PATENTS

- US Patent # 4,983,393, January 8, 1991 - Intra vaginal device and methods for sustained release.
- US Patent # 5,069,906, December 3, 1991 - Intra-vaginal device method

PARACETAMOL PATENTS

- PCT # 200002653, filed March 11, 2000. New dispersible and soluble galenic formulation of paracetamol, process for its preparation and applications.

OMEPRAZOLE PATENTS

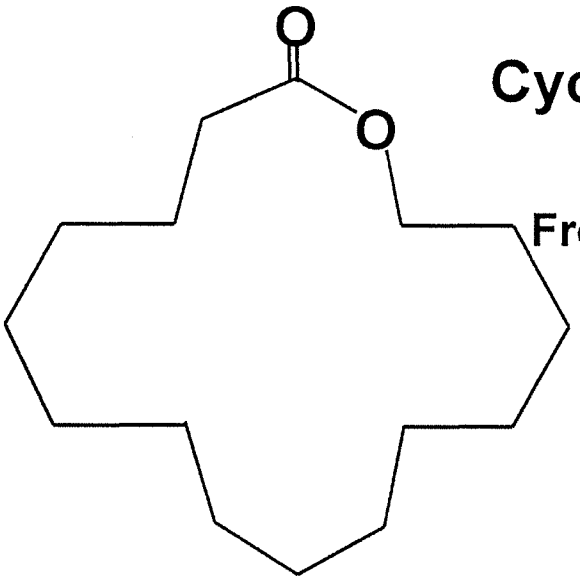
- PCT # P200100825, filed April 6, 2001 - Process for manufacture of stable and gastro-resistant pellets of omeprazole and other pharmaceutical products
- PCT # P200002797, filed November 22, 2000 - New galenic formulations of omeprazole in tablet form, procedure for the process and application in human and veterinary medicine.

ORAL DELIVERY

- PCT # P200002685, filed November 7, 2000 - Procedure for the vacuum production and preparation of pharmaceuticals for liberation and protection from gastro-degradation.

Bentley Topical Drug Delivery

Bentley Permeation Excipient



Cyclopentadecanolide (CPE-215)
Oil of Angelica Essence

From the root of Angelica archangelica